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(54) Title: METHOD FOR IDENTIFYING CELLULAR GROWTH INHIBITORS

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(57) Abstract: The present invention is a method which permits the selective screening for growth-inhibiting substances having a known mechanism of action; i.e., substances which inhibit or otherwise interfere with an enzyme or other gene product whose function is required for the growth or survival of the cell. The method employs cells (e.g., bacterial cells) that contain a nucleic acid fragment that encodes an RNA fragment that can interfere with the expression of a gene product (e.g., an anti-sense RNA that hybridizes to a mRNA), wherein expression of the RNA fragment pre-sensitizes the cell to substances (drugs) that act at the gene product (e.g., a protein or RNA). The cells lose the capability to express the RNA fragment. In the method, the recombinant cells are grown in a nutrient medium in the presence of a test substance under conditions in which expression of the RNA fragment occurs at a level that pre-sensitizes the cell to substances that act at the targeted gene product. The growth conditions are also controlled such that the cells lose the capability to express the RNA fragment. When the test substance is a growth inhibitor that acts on the targeted gene product, the cells lacking the RNA fragment (revertant cells) will have a growth advantage over cells containing the RNA fragment, and the growth of revertant cells will occur. The method of the invention includes monitoring the cell growth for the appearance of revertant cells, which leads to the identification of selective growth inhibitors having a specific mode of action.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68, 1/02, 1/18; C12N 1/20, 15/00; C07H 21/04
 US CL : 435/5, 29, 32, 172.3, 252.3, 320.1; 536/24.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. :

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
DIALOG, WEST, MEDLINE**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,821,052 A (CHEN et al) 13 October 1998, see entire document.	1-31
A	DeVito et al. An array of target-specific screening strains for antibacterial discovery. Nature Biotech. May 2002, Vol. 20. No. 5, pages 478-483, see entire document.	1-31

 Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"O" document referring to an oral disclosure, use, exhibition or other means		
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